Matthew B. Van Hook
DEPUTY GENERAL COUNSEL

PhRMA

November 4, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: Proposed Rule – 180-day Generic Drug Exclusivity for Abbreviated New Drug Applications, 21 C.F.R. Part 314
64 Fed. Reg. 42873 (August 6, 1999), Docket No. 85N-0214

Dear Madam or Sir:

The Pharmaceutical Research and Manufacturers of America ("PhRMA") represents the country's leading research-based pharmaceutical and biotechnology companies. PhRMA member companies are investing nearly 24 billion dollars in 1999 alone in discovering new medicines that greatly improve the public health and lives of patients and their families. This substantial commitment to discovering new medicines depends on strong intellectual property protection.

The Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman Act") has an important impact on the intellectual property protection for innovative pharmaceutical products. The principal focus of the Hatch-Waxman Act was to create a system to facilitate generic drug competition. The generic drug provisions of the Hatch-Waxman Act permit the generic applicant to reference the safety and efficacy data of the innovator company, thereby avoiding the risk and expense of demonstrating safety and efficacy of the generic product. Congress realized, however, that the significant restrictions on the pioneer's exclusive use of the safety and efficacy data took valuable intellectual property rights from pioneer companies. Accordingly, the Hatch-Waxman Act also included an incentive for product innovation. This incentive provides for the partial restoration of patent terms that have been eroded due to the required safety and efficacy testing and FDA review.

The Hatch-Waxman Act represents a political compromise to balance the competing interests of pioneer product innovation and generic drug competition. Likewise, the regulations implemented under the Hatch-Waxman Act have a substantial impact on the balance

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Pharmaceutical Research and Manufacturers of America
1100 Fifteenth Street, NW, Washington, DC 20005 • Tel: 202-835-3513 • FAX: 202-835-3592 • E-MAIL: mvanhook@phrma.org

between these competing interests. Accordingly, PhRMA member companies have a vested interest in any regulatory proposal that is intended to affect generic drug marketing because it can distort the congressionally intended balance between the incentives for innovation and generic drug competition.

On August 6, 1999, the Food and Drug Administration ("FDA") proposed a change in the regulation governing the Hatch-Waxman provision that provides a period of generic drug market exclusivity during which the first generic applicant to challenge a pioneer patent can market its product without competition from generic competitors. See *180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications*, 64 Fed. Reg. 42873 (1999) (to be codified at 21 C.F.R.§314) (hereinafter referred to as the "Notice" for the discussion, and "Proposed Rule" for the proposed regulation). The award of a 180-day period of market exclusivity for certain applicants that file Abbreviated New Drug Applications ("ANDAs") with paragraph IV certifications[1] was enacted by Congress as an essential element in the balance between generic competition and pioneer product innovation. The Notice alleges, however, that the intended balance between these competing interests has been upset through the establishment of certain agreements between generic and innovator companies that may have the effect of substantially delaying the entry of competitive drug products into the market. In order to prevent the alleged delay in the market entry of multiple generic drug products, FDA proposes to impose significant limitations on the circumstances in which the 180-day period of market exclusivity would be available.

As described in the comments below, PhRMA believes that the Proposed Rule is inconsistent with the statutory provisions and, thereby, upsets the balance established by Congress in the Hatch-Waxman Act. First, the Proposed Rule would change the 180-day exclusivity provision from being patent-specific to being product-specific. This change would substantially alter the impact of the 180-day exclusivity provisions on products with multiple patent listings. Second, the Proposed Rule establishes a "triggering period," a new period of 180 days during which the statutory exclusivity period must start. If the statutory exclusivity does not start during the triggering period, the first applicant will lose its exclusivity. This newly defined period creates numerous circumstances which destroy the 180-day exclusivity period that was created by statute.

Each of these elements of the Proposed Rule upsets the balance established by Congress because neither is consistent with the statutory language or policy objective of the 180-day exclusivity provision. Accordingly, the Proposed Rule should be revised to be consistent with the statutory language in the Hatch-Waxman Act.

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[1]A paragraph IV certification refers to a certification by the generic applicant that the patent listed for the pioneer product is invalid, unenforceable, or not infringed. See Section 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act.

Summary of Suggested Changes to the Proposed Rule

The Proposed Rule creates multiple circumstances in which the first ANDA applicant is denied the benefit of 180 days of exclusive marketing (1) because, under the Proposed Rule, the marketing exclusivity begins before FDA has the authority to approve the ANDA, (2) because, under the Proposed Rule, the marketing exclusivity begins before the ANDA is ready for approval, or (3) because, under the Proposed Rule, ongoing litigation or the threat of compensatory and enhanced damages prevents the marketing of the product even though the exclusivity period has begun. By limiting the ability of the first applicant to be able to market its product during the period of exclusivity, FDA ignores the congressional intent to provide 180 days during which the first applicant can market its product without competition from other generic manufacturers.

The Proposed Rule limits the availability of 180-day generic drug exclusivity by (a) changing 180-day exclusivity from being patent-specific to being product-specific, and (b) establishing a triggering period that creates additional circumstances in which the first paragraph IV ANDA applicant is denied 180 days of marketing exclusivity. In limiting the availability of generic drug exclusivity, FDA's proposal circumvents the statutory and policy objective of the 180-day exclusivity provision. Accordingly, the Proposed Rule should be revised: (a) to maintain the current patent-specific award of 180-day market exclusivity, as provided by the relevant statutory provision; and (b) to eliminate the proposed "triggering period," the newly created hurdle to the award of 180-day market exclusivity that is not authorized by statute.

I. The Proposed Rule Should be Revised to Maintain the Current Patent-Specific Award of 180-Day Market Exclusivity.

Since its enactment, the 180-day generic drug exclusivity provision has been interpreted to apply to each listed patent for each drug product. In contrast to the current practice, FDA's Proposed Rule would apply 180-day exclusivity on a product-specific basis. That is, the exclusivity would be awarded only once for any product based on a paragraph IV certification for any listed patent for the product. As described below, this approach reduces substantially the circumstances in which the first paragraph IV ANDA applicant can benefit by marketing its product without competition from other generic products, as intended by Congress.

A. The Statutory Language Requires the Patent-Specific Award of 180-day Exclusivity.

The relevant statutory language requires a patent-specific analysis of paragraph IV certifications and the corresponding 180-day generic drug exclusivity. As provided in the Hatch-Waxman Act, an ANDA must contain:

> a certification, in the opinion of the applicant and to the best of his knowledge, ***with respect to each patent*** which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for

> which information is required to be filed under subsection (b) and (c) of this section -
>
> > (I) that ***such patent*** information has not been filed,
> > (II) that ***such patent*** has expired,
> > (III) of such date on which ***such patent*** will expire, or
> > (IV) that ***such patent*** is invalid or will not be infringed by the manufacturer use or sale of the new drug for which the application is submitted; . . ..

21 U.S.C.§ 355(j)(2)(A)(vii)(emphasis added). Accordingly, the patent certifications are patent-specific.

Additionally, the statutory basis for the 180-day exclusivity period requires a patent-specific analysis in order to determine entitlement to the exclusivity period.

> If the [subsequent ANDA] contains a certification described in subclause IV of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection [containing] ***such a certification***, the application shall be made effective not earlier than one hundred and eighty days after —
>
> > (I) the date the Secretary received notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or
> >
> > (II) the date of a decision of a court in an action described in clause (iii) holding ***the patent which is the subject of the certification*** to be invalid or not infringed whichever is earlier.

21 U.S.C. § 355(j)(5)(B)(iv)(emphasis added). Accordingly, the statutory language requires reference to the patent-specific paragraph IV certification of the subsequent ANDA to determine whether its approval must be delayed by 180 days because of a previous ANDA containing such a patent-specific certification. A patent-specific paragraph IV certification to a different patent could not be considered "such a certification."

In contrast to the statutory requirement for the award of 180-day exclusivity on a patent-specific basis, FDA proposes to change policy and practice to award 180-day exclusivity on a product-specific basis. Throughout the Notice, FDA emphasizes that the 180-day exclusivity will be product-specific. The Notice includes comments, such as:

> "[O]nly the applicant submitting the first substantially complete ANDA for a listed drug with a paragraph IV certification to any patent in the Orange Book for the listed drug (first applicant) would be eligible for exclusivity."[2]
>
> "An applicant must be the first to submit an ANDA that is both substantially complete and contains a paragraph IV certification to any listed patent."[3]
>
> "If there are multiple patents for the listed drug, the applicant submitting the first paragraph IV certification to any of the listed patents will be the only ANDA applicant eligible for exclusivity for that drug."[4]

These statements confirm that product-specific 180-day exclusivity would permit a generic applicant to submit an ANDA containing a single paragraph IV certification (for a product with multiple listed patents), thereby destroying the ability of any other ANDA applicant to obtain 180 days of marketing exclusivity for submitting a paragraph IV certification to one of the other patents. Based on this change alone, the Proposed Rule circumvents the 180-day exclusivity provision by limiting substantially the circumstances in which generic drug marketing exclusivity is awarded.

B. FDA Fails to Articulate Any Concern that Justifies a Change from the Patent-Specific Award of 180-Day Exclusivity.

In the Notice, FDA rejected the patent-specific approach to 180-day exclusivity based principally on its concern about the application of patent-specific exclusivity when multiple patents are listed for a product.

> The agency considered an approach that could have made multiple applicants eligible for exclusivity based upon the order of submission of paragraph IV certifications for each patent. Different ANDA's are most likely to have the first paragraph IV certifications to different patents when new patents are listed for the innovator drug after the submission of the first ANDA. Although the statute would support granting multiple exclusivities, the agency has determined that such multiple exclusivities for a single drug could further delay the entry of generic drugs onto the market.

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[2]Notice, 64 Fed. Reg. at 42,873.

[3]*Id.*

[4]*Id.*

Notice, 64 Fed. Reg. at 42,876. Despite FDA's concerns about granting multiple patent-specific exclusivities, the agency cannot ignore the patent-specific requirements of the statutory provision. Moreover, as described below, FDA's concerns about multiple patent-specific exclusivities are not justified.

In the case of a product with multiple patent listings and the potential for multiple paragraph IV certifications, the patent-specific approach to 180-day exclusivity would preserve the benefit of 180 days of exclusive marketing. Under FDA's regulations, the ANDA would not be approved until the last certification was resolved.[5] If there were no injunction, FDA could approve the product at the end of the 30-month stay. Alternatively, if the court issued an injunction in the patent infringement suit that prevented the marketing of the product, FDA would not approve the product until a court determined that the patent was invalid, unenforceable or infringed. In either case, under a patent-specific analysis application of the patent-specific 180-day exclusivity provision would result in no more than a single 180-day period of exclusive marketing for a drug product. Under the patent-specific approach, the 180 days of marketing exclusivity would begin after the resolution of the last paragraph IV certification, thereby permitting the first applicant to enjoy the benefit Congress intended -- 180 days of marketing without competition from other generic competitors.

Nevertheless, FDA maintains that a patent-specific approach to 180-day exclusivity is "virtually unworkable in its complexity"[6] in light of the relative ease with which an applicant becomes eligible for exclusivity.[7] According to FDA,

> if two different applicants were eligible for exclusivity because each was the first to file a paragraph IV certification for a different listed patent, and neither exclusivity could begin to run until first commercial marketing or a favorable court decision, it is possible that each exclusivity would block the final approval of the other application for a substantial period of time.

Notice, 64 Fed. Reg. at 42,875. Even in the circumstances in which the patent-specific approach would award exclusivity to more than one party, the exclusivity of one ANDA applicant could not block the approval of the other ANDA applicant for more than 180 days. Similarly, the dual exclusivities could not block subsequent applicants for more than 180 days after a triggering event. Accordingly, FDA's asserted concerns about the award of 180-day exclusivity on a patent-specific basis do not justify the proposed change to a product-specific approach to awarding 180-day exclusivity.

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[5]21 C.F.R. §314.107 (b)(4) provides that ANDA product will be approved upon the resolution of the last patent certification.

[6]Notice, 64 Fed. Reg. at 42,875.

[7]*Id.*

The Proposed Rule would have a detrimental effect on products with multiple patent listings. The product-specific approach to 180-day exclusivity would permit the resolution of one paragraph IV dispute to destroy exclusivity for the remaining paragraph IV disputes that are likely to be determinative for marketing a generic product. In all cases of multiple patent listings, the patent-specific approach to awarding 180-day exclusivity follows the intent of the statutory language while FDA's proposed product-specific approach does not follow statutory intent.

II. The Proposed Rule Establishes a Triggering Period that is Neither Authorized by Statute Nor Consistent with the Policy Objectives of the 180-Day Exclusivity Provision.

The Proposed Rule establishes a period of 180 days during which one of the statutory trigger events must occur. This new 180-day period is defined as the "triggering period." If a triggering event does not occur during the triggering period, then the first applicant that submitted an ANDA containing a paragraph IV certification is no longer eligible to receive 180 days of marketing exclusivity. Moreover, no other ANDA applicant that had filed a paragraph IV certification would be eligible for 180-day exclusivity.[8]

According to the Notice, the triggering period is necessary to prevent indefinite delays in generic drug competition that could result from settlement agreements or failure of the first paragraph IV ANDA applicant to promptly obtain approval or market its product. Despite this concern, the triggering period limits the opportunities for 180-day exclusivity, thereby circumventing the statutory language enacted by Congress.

The triggering period would establish, in most circumstances, a period of 180 days following certain defined events, during which the triggering events must occur.

> In most cases, the triggering period would begin to run on the day a subsequent ANDA applicant with a paragraph IV certification receives a tentative approval stating that but for the first applicant's exclusivity, the subsequent ANDA would receive final approval. In three instances the triggering period would not begin to run on the date of the tentative approval.
>
> First, if the first applicant was sued for patent infringement as a result of its paragraph IV certification and the litigation is ongoing, the triggering period would not begin until expiration of the 30-month stay of ANDA approval . . . Similarly, if a court issued a preliminary injunction prohibiting the first applicant from commercially marketing its drug product, the triggering period would not begin until the injunction expired. Finally, the triggering period would not begin

[8]Under the proposed product-specific rule, the ineligibility of the first applicant would destroy 180-day exclusivity for any other applicant for the product even if the certifications were not for the same patents.

> until expiration of the statutorily described time period corresponding with any existing exclusivity periods for the listed drug (see sections 505(j)(5)(D)(ii) and 505A(a) of the act).

Notice, 64 Fed. Reg. at 42,877.

Accordingly, the triggering period creates the great possibility that the 180-day exclusivity can be triggered for the first ANDA applicant: (1) during the 30-month stay; (2) prior to approval of the first ANDA; (3) during district court litigation; or (4) during the appeal process. As the agency has recognized in the past, beginning the 180-day exclusivity during any of these times would "render the exclusivity valueless."[9]

FDA acknowledges that in some circumstances the first ANDA applicant might be unable or unwilling to market its product at the time of a court decision trigger in a case for another applicant. In this regard, the agency states "that in such a situation the first applicant may obtain a financial benefit from the award of exclusivity by waiving its exclusivity with respect to a subsequent applicant . . .." A hypothetical financial benefit is not equivalent to the statutory benefit that Congress determined was appropriate in the balance of interests between generic competition and pioneer product innovation.

The Notice asserts that the length of the triggering period is derived from the statutory provision governing 180-day exclusivity. According to the Notice,

> [t]his provision quite clearly allows (and Congress, therefore, presumably contemplated) the possibility of a 180-day period during which there is no generic drug product on the market. This would occur when the running of the 180-day period of exclusivity has begun with a court decision finding the patent invalid, unenforceable, or not infringed, but the applicant that has the exclusivity does not begin marketing its product because it is not approved or for another reason.

Id. at 42,878. This rationale, however, does not support a 180-day triggering period over a triggering period of any other length.

In establishing the period of exclusive generic marketing, Congress enacted a provision that acknowledges or requires two periods of delay in subsequent generic drug approval. First, the Hatch-Waxman Act recognizes that subsequent generic drug approval will not occur until the first ANDA applicant either markets its product or a court rules that the relevant patent is invalid, unenforceable, or not infringed. Second, the Hatch-Waxman Act creates a delay of 180 days in which other ANDA patent challengers are precluded from marketing their products. However, instead of focusing on providing 180 days of exclusivity for

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[9] *Abbreviated New Drug Application Regulations; Patent and Exclusivity Provisions; Final Rule*, 59 Fed. Reg. at 50,352.

the first ANDA applicant, as does the statute, the Proposed Rule is focused on limiting to 180 days that time during which a subsequent applicant is prevented from marketing its product due to another applicant's exclusivity.

FDA's attempt to justify a triggering period of 180 days (or a triggering period of any definite length) requires FDA to ignore that Congress created a different statutory scheme that did not contemplate a definite period without competition from a subsequent generic applicant.[10] Accordingly, FDA's proposal fails to conform to the statutory regime for generic drug exclusivity established by Congress, and the Proposed Rule must be revised to eliminate the statutorily unauthorized "triggering period."

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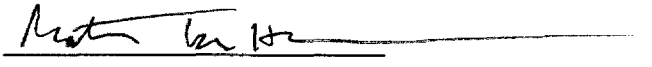
PhRMA appreciates the opportunity to comment on this Proposed Rule. PhRMA and its member companies encourage the FDA to revise the Proposed Rule to comply with the statutory language of the Hatch-Waxman Act.

Sincerely,



Matthew B. Van Hook

[10]The arbitrariness of the length of the triggering period is confirmed by the proposal for a reduced triggering period of 60 days in some cases.